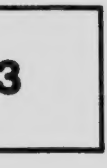

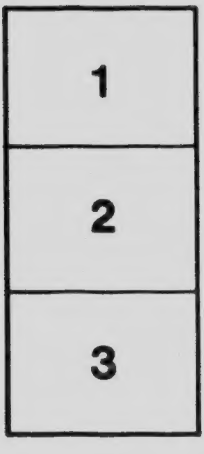

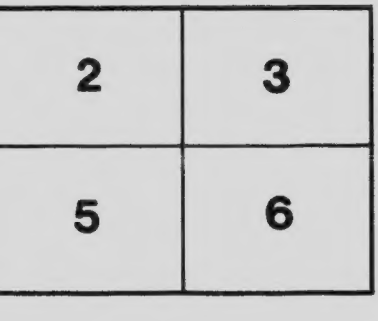

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No. 28: THE ACTION OF ADRENALIN ON THE KIDNEY.
BY FRANK A. HARTMAN and ROSS S. LANG

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THE ACTION OF ADRENALIN ON THE KIDNEY

Frank A. Hartman and Ross S. Lang.

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Many investigators have studied the action of adrenalin on the kidney, both in regard to circulatory changes and to urine flow, and have found that one or both may be modified by this substance. Inasmuch as Cow (1) has shown that there is direct communication between the adrenal medulla and certain parts of the kidney, it appears that adrenalin might have some important function in the control of the kidney. In the present instance we have made a study of the influence of adrenalin on the kidney volume, both from gangliar and peripheral action. Although it is possible that adrenalin may influence urinary secretion independent of vascular changes, yet we know that if vascular changes occur they will also modify kidney activity. It is assumed that volume changes are due to vascular changes.

METHODS.

The methods employed were similar to those used in a previous study of the spleen (2), the kidney being enclosed in a gutta percha oncometer which was connected with a Brodie bellows recorder.

In the perfusions the vessels were all tied off and warm oxygenated Ringer's solution forced into the renal artery under a constant pressure. Injections of adrenalin into the perfusion fluid were made at the entrance of the perfusion cannula by means of a hypodermic needle piercing the rubber tubing. Passive effects of the injection were ruled out either by slow injection or else by a simultaneous removal of an equal quantity of perfusion fluid by another needle inserted farther back in the connecting rubber tube.

All animals were under the influence of ether. Adrenalin solutions were made by diluting Parke, Davis & Co.'s adrenalin chloride solution with distilled water.

RESULTS.

In an earlier research (3) we found that small doses of adrenalin injected into the general circulation caused constriction of the kidney, while in some instances larger doses caused

constriction followed by dilatation. Brief dilatation preceding constriction occurred at times, but appeared to be a passive result from a short rise in blood pressure.

Five more cats and three dogs were studied in this way, with results which agree with the earlier research.

One experiment may be cited. The kidney of a dog weighing 18 kgm. responded by constriction to doses of adrenalin ranging from 0.2 cc., 1:100,000 to 0.4 cc., 1:10,000. These were all depressor doses of adrenalin. The response to doses ranging from 0.4 cc., 1:10,000 to 3.0 cc., 1:10,000 was constriction followed by dilatation (Fig. 1); 0.6 cc., 1:10,000 was a depressor dose, while 1.3 cc. of the same dilution was pressor in effect.

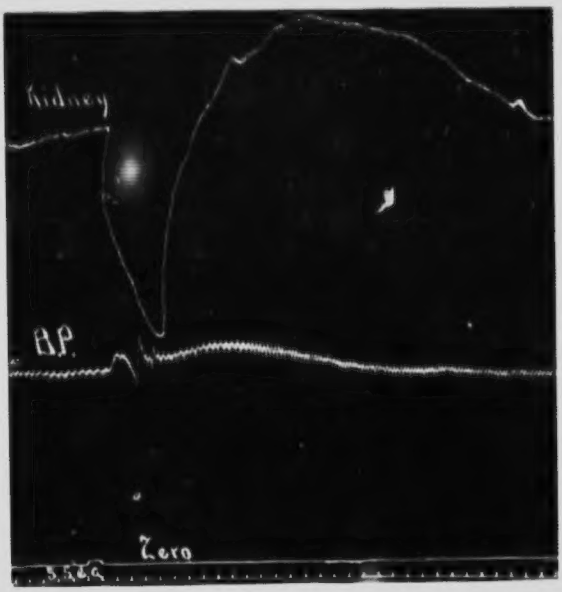

Fig. 1. Constriction and dilatation of a normal kidney from adrenalin, 1.3 c.c., 1:10,000 injected into the jugular vein. Dog 18 kgm.

Although this delayed dilatation occurring in the kidney was similar to that occurring in the intestines (3, p. 313) with large doses of adrenalin it was by no means so prevalent. However, in those individuals in which it was obtained it resulted repeatedly from injections above a certain dose.

We next attempted to locate the regions where adrenalin could produce these two effects, i. e., constriction and dilatation. In order to separate peripheral from gangliar or more central effects, we completely cut off the kidney from the body circulation, then perfused it. Nervous connections to the kidney were carefully preserved in the operation. Both kidneys were perfused alternately in two dogs. The first was an animal (18 kgm.) that gave constriction followed by dilatation of the kidney when its circulation was intact and a large dose of adrenalin was injected into the jugular vein. When perfused, the left kidney gave dilatations from jugular vein injections of doses above 0.2 cc., 1:10,000. Sometimes slight constriction preceded the dilatation (Fig. 2). Injections of adrenalin into the perfusion

Fig. 2. Constriction and dilatation of a perfused kidney, 2 c.c., 1:10,000 adrenalin injected into jugular vein. Dog 18 kgm.

fluid caused a similar effect, i. e., constriction followed by dilatation (Fig. 3). Occasionally the dilatation was followed by constriction. The other kidney responded in a similar manner, both before and after perfusion.

The second dog (15 kgm.) gave dilatation in both perfused kidneys from adrenalin injected into the jugular vein, while injections into the perfusion fluid caused constriction (Fig. 4). Doses as small as 0.2 cc., 1:100,000 gave this result.

Volume changes in perfused kidneys from jugular vein injections of adrenalin, may be due to action on structures in the semilunar ganglion, dorsal root ganglia or in some more central location. We tried the effect of direct application of adrenalin to these

ganglia. The ganglia were usually slit to facilitate absorption. In the case of the semilunar ganglion, the mesentery was cut and separated from it in such a way that a pocket could be made

Fig 3. Constriction and dilatation of a perfused kidney from the injection of 0.2 c.c., 1:100,000 adrenalin into the perfusion fluid. Dog 18 kgm.

Fig. 4. Constriction of a perfused kidney from the injection of 1.3 c.c. 1:100,000 adrenalin into the perfusion fluid. Dog 15 kgm.

by engaging the cut surface of the mesentery with haemostats. Adrenalin solutions could then be confined in this pocket without absorption into the general circulation.

Adrenalin action on the semilunar ganglion was studied in three cats and one dog. Dilatation of the kidney was obtained in all of these when adrenalin was applied to the ganglion in question. In some animals, concentrations as low as 1:100,000 produced this result; in others a 1:10,000 solution was necessary (Fig. 5). In two of the cats the latter solution sometimes caused

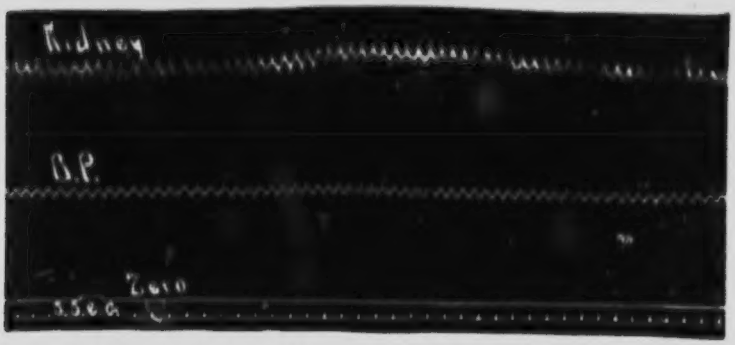

Fig. 5. Dilatation of the kidney caused by the application of 1:10,000 adrenalin to the semilunar ganglion. Cat. 3.1 kgm.

dilatation followed by constriction. This could be explained on the ground that small amounts of absorbed adrenalin affect the dilator mechanism, while larger amounts bring the constrictor mechanism into action. This was confirmed by the pure constriction which it was possible to obtain with concentrated adrenalin solutions (1:1,000) (Fig. 6).

We concluded from these observations that adrenalin can influence the volume of the kidney by action upon both dilator and constrictor mechanisms located in the semilunar ganglion, the result depending upon the concentration of adrenalin absorbed.

The effect of adrenalin through the dorsal root ganglia was studied in four cats. With the animal lying on its side, an opening extending transversely from the midline was made in the abdominal wall above the kidney. The kidney was placed in the oncometer and the apparatus properly adjusted before exposure of the dorsal root ganglia. The twelfth and thirteenth thoracic ganglia were carefully exposed and their connections with the spinal cord severed. After allowing a short time for the bleeding to stop, the adrenalin solution was applied to a ganglion. In

some cases, to make sure that adrenalin was not escaping into the general circulation, the ganglion was surrounded by rubber dam. The earlier the adrenalin was applied the more sensitive was the ganglion. In fact, if the ganglion had been exposed too long or the blood pressure had become extremely low, there was

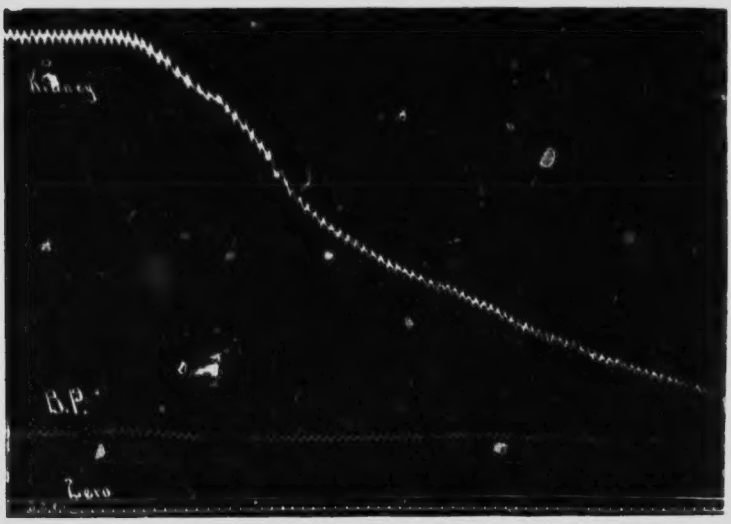

Fig. 6. Constriction of the kidney caused by the application of 1:1,000 adrenalin to the semilunar ganglion.

either no response or else only a slight effect. Second and third applications to the same ganglion had no effect unless several minutes intervened and the ganglion was thoroughly washed with isotonic salt solution. The adrenalin solution was warmed to 37° C. because cold solutions of distilled water sometimes produced an effect.

In one animal, constriction of the kidney was produced by 1:10,000 adrenalin applied to the dorsal root ganglia. No dilatation was obtained. The blood pressure, however, was quite low (32 mm.).

Dilatation of the kidney was produced in the three remaining animals from solutions of 1:10,000. One of these animals gave a similar response with 1:100,000 adrenalin. The response is frequently very slow, due no doubt to the slow absorption by the ganglion (Fig. 7).

Fig. 7. Dilatation of the kidney produced by painting a dorsal root ganglion with 1:10,100 adrenalin. The ganglion was surrounded by rubber dam. Cat 2.4 kgm.

DISCUSSION.

Our experiments prove that adrenalin frequently causes dilatation of the kidney. This dilatation can be caused by action on the semilunar ganglion, dorsal root ganglia, or, in some cases, on structures in the kidney itself.

Hoskins and Gunning (4) obtained dilatation following constriction in one dog out of sixteen from intravenous doses. This has been more frequent in our experiments, as five out of nine gave this response. In addition to these experiments, which were upon kidneys with an intact circulation, we have obtained dilatation of the perfused kidneys of two dogs.

Kidney dilatation from small doses of adrenalin may be more common than one might suppose. However, the constrictor mechanism in the kidney tends to predominate in adrenalin responses.

In view of the recent work of Addis, Barnett and Shevky (5) we tried to obtain dilatation of the kidney in a rabbit by the application of adrenalin to the semilunar ganglion. Concentrations of adrenalin from 1:100,000 to 1:10,000 caused only constriction in the kidney. This is confirmatory of recent work from this laboratory (6), which has shown that rodents are exceptional among mammals in that adrenalin vasodilator mechanisms are either absent or else insignificant in their action.

We also attempted to produce volume changes in the kidneys of cats by subcutaneous injection of adrenalin. Doses of 0.5 cc., 1:1,000 produced no distinct result. Three animals were tested in this way. Therefore, it seems that even in animals which are known to possess adrenalin vasodilator mechanisms subcutaneous injections have little effect upon the volume of the kidney.

In regard to the effect of adrenalin mingled with the perfusion fluid fed to a kidney, numerous observations have been made by others. Sollmann (7), with relatively large doses of adrenalin, obtained constriction. He says, however, that after several hours' perfusion, or sometimes earlier, the constrictor action disappears and that at times it is replaced by a dilator action. Pari (8) obtained one case of dilatation from adrenalin in the perfused kidney.

SUMMARY.

1. Adrenalin in moderate amounts produces dilatation of the kidney in some individuals.
2. Dilatation is usually preceded by a brief constriction.
3. Adrenalin can produce dilatation by its action on either the semilunar ganglion, dorsal root ganglia, or on some structure in the kidney.
4. Likewise constriction can be produced by adrenalin acting either in the semilunar ganglion, dorsal root ganglia, or the constrictor structures in the kidney.

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